REMARKS

Upon entry of this amendment, claim 1 is pending in the instant application. Claim 1 has been amended herein. Support for the amendments to claim 1 can be found throughout the specification, *e.g.*, at page 32, lines 8-14 and 27-33; and at page 35, line 13, and in claim 1, as originally filed. Thus, no new matter has been added by this amendment.

Claim Rejections – 35 U.S.C. § 112

The Examiner has rejected claim 1 under 35 U.S.C. § 112, second paragraph as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner has indicated that the recitation of "a biocompatible matrix formed of a hydrogen" in claim 1 is indefinite because it is unclear how a matrix is formed from one hydrogen. (*See* Office Action at page 2). Applicants thank the Examiner for pointing out this typographical error in claim 1. This claim has been amended herein to recite the phrase "a biocompatible matrix formed of a hydrogel". Support for this amendment is found at least at page 35, line 13 of the specification. Thus, Applicants submit that this rejection should be withdrawn.

The Examiner has also indicated that "[t]he recitation of 'substantially free of direct ionic bonding' is vague and indefinite. The numerical parameter of 'substantially free' is unclear since the specification does not provide a definition." (Office Action at page 2). Applicants have herein amended claim 1 to remove this recitation. As amended herein, claim 1 now specifies that "the hydrogel material does not ionically bond to a polymer of opposite charge on the core during formation of the jacket . . ." Support for this amendment is found at least at page 32, lines 8-14 and 27-33 of the instant specification. Thus, Applicants submit that claim 1, as amended herein, is neither vague nor indefinite. As such, this rejection should be withdrawn.

For these reasons, Applicants contend that the rejection of claim 1 under 35 U.S.C. § 112, second paragraph, has been overcome.

Claim Rejections--35 U.S.C. § 103

Claim 1 has been rejected under 35 U.S.C. § 103(a) as being unpatentable over United States Patent No. 4,997,443 ("Walthall") in view of United States Patent No. 4,353,888 ("Sefton"). According to the Examiner,

> [i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Walthall et al and Sefton and utilize Sefton's polymeric membrane to further encapsulate the implantable cells. One would have been motivated to do so since Sefton teaches the use of the polymeric membrane not only provides the cells with sufficient nutrients and allows the passage of the cells' secretions, but it also protects the implant from the host's immune system by preventing the diffusion of the host's antibodies into the implant. Therefore, since Walthall recognizes the criticality of preventing cell immune response to the implant while simultaneously providing nutrients to the implant, one would be motivated to look to Sefton, who provides the solution to this problem using a semipermeable membrane.

(Office Action at pages 3-4). Applicants traverse.

Applicants contend that the Examiner has failed to establish a *prima facie* case of obviousness. A *prima facie* case of obviousness requires some suggestion or motivation, either in the references themselves or in the knowledge generally available in the art, to modify the references or to combine reference teachings. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *See* MPEP 706.02(j).

Claim 1 has been amended herein to clarify that the claimed implantable, immunoisolatory vehicle is a macrocapsule rather than a microcapsule. Specifically, claim 1 now recites that the vehicle has a core comprising a volume in excess of 1 μl and at least about 10^4 living cells dispersed in a biocompatible matrix. In contrast, as noted in the instant specification, microcapsules "have a typical maximum practical volume on the order of 1μl". (Specification at page 40, lines 19-20). Moreover, "[t]he droplet methods used in the making of microcapsules, in order to ensure cell viability, necessarily limit the number of cells per capsule to fewer than 10^4." (Specification at page 41, lines 29-32).

As acknowledged by the Examiner, Walthall does not teach an external diffusion jacket. (*See* Office Action at page 3). However, the Examiner contends that one of ordinary skill in the art would have been motivated to combine the teachings of Sefton, which describes implantable mammalian cells that are encapsulated in a polymeric membrane, with the teachings of Walthall in order to arrive at the implantable immunoisolatory vehicles of the instant invention. (*see* Office Action at pages 3-4). Applicants disagree with the Examiner's contention.

Sefton describes microencapsulated, viable mammalian cells in a form suitable for use in medical treatment. (*See, e.g.*, Sefton at col. 1, lines 5-7; col. 2, lines 15-19). There is no teaching or suggestion in Sefton of macroencapsulated cells. In fact, Sefton specifies that the invention described therein "provides small beads comprising a few viable cells . . ." (Sefton at col. 1, lines 64-66). In contrast, as noted, amended claim 1 requires that the core of the claimed vehicle comprise at least about 10^4 living cells. Thus, Applicants submit that the microencapsulation techniques described in Sefton are different from the macroencapsulation techniques of the instant invention.

The instant specification describes the differences between the claimed macrocapsules and the microcapsules described in the prior art (including Sefton), as well as the advantages of using the claimed macrocapsular implantable vehicles. (*See* page 40, line 15 through page 41, line 32). These differences make it clear that the claimed macrocapsules address many of the limitations observed with prior art microcapsules. Thus, Applicants contend that one skilled in the art would have no motivation to combine the microencapsulation teachings of Sefton with those of Walthall in order to create the claimed implantable, immunoisolatory, macrocapsular vehicles. Moreover, contrary to the Examiner's contention, Applicants submit that the ordinarily skilled artisan would not look to the polymeric membrane described in Sefton for use in microcapsules to solve the problem of preventing cell immune response to the implant while simultaneously providing nutrients to a macrocapsular implant.

Thus, Applicant contends that claim 1, as amended herein, is not obvious over Walthall in view of Sefton. Therefore, this rejection should be withdrawn.

Double Patenting

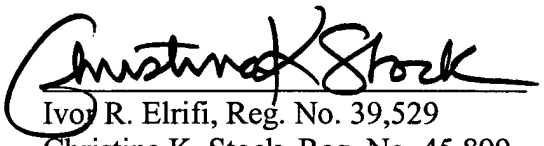
The Examiner has also rejected claim 1 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent Nos. 5,800,828; 6,083,523; 5,955,095; and 6,322,804.

In response, Applicants submit herewith terminal disclaimers over each of these U.S. Patents along with the corresponding fee under 37 C.F.R. § 1.20(d). Therefore, this rejection is moot and should be withdrawn.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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